REMARKS

Claims 1-71 are all the claims pending in the application; claims 33-58 and 63-71 have been withdrawn from consideration; claims 1-32 and 59-62 are under consideration; claims 1-15, 17-32, and 59-62 have been rejected; claim 16 has been allowed.

Upon entry of this amendment, claim 61 will be canceled and claims 1-60 and 62-71 will be pending.

Support for the amendment of paragraphs [173], [175], [178] and [201] to correct the term "5 ?" to be "5 Å," and the term "IgV?" to be "IgVκ", can be found in the provisional application at paragraphs [172], [174], [177] and [200], respectively.

Included herewith is a substitute Sequence Listing wherein the amino acid sequences in Figures 8A and 8B have been added to the Sequence Listing. Entry of the substitute Sequence Listing is respectfully requested.

The Brief Description of the Drawings has been amended to insert the sequence identifiers for the two new sequences added to the Sequence Listing.

Claims 59 and 60 have been amended to recited antibodies having "increased binding affinity" for CD33 compared to a first antibody. Support for the amendments may be found, *e.g.*, in claim 61, and the specification at page 7, paragraph 31, and at page 18, paragraphs 95-99.

Support for the additional amendments to claims 59 and 60 may be found at page 18, paragraphs 95 to 99.

The amendment to the claims to recite antibodies that "specifically" bind CD33 may be found throughout the specification, such as in paragraph 13.

No new matter has been added. Entry of the Amendment is respectfully requested.

I. Objections to the Specification

A. At paragraph 5 of the Office Action, the Abstract has been objected to because it uses the legal phraseology "said antibodies."

Included herewith is an amendment to the Abstract wherein the legal phraseology has been deleted. In view of the amendment to the Abstract, reconsideration and withdrawal of this objection is requested.

B. At paragraph 6a of the Office Action, the specification has been objected to because it contains a hyperlink in paragraph [171].

Included herewith is an amendment to the specification wherein the hyperlink has been deleted. In view of the amendment to the specification, reconsideration and withdrawal of this objection is requested.

C. At paragraph 6b of the Office Action, the specification has been objected to due to the term "5 ?" in paragraphs [173], [175] and [178]. The specification has further been objected to due to the term "IgV?" in paragraph [201].

Included herewith is an amendment to the specification wherein the term "5 ?" has been corrected to "5 Å," and the term "IgV?" has been corrected to "IgVκ". In view of the amendment to the specification, reconsideration and withdrawal of this objection is requested.

D. At paragraph 6c of the Office Action, the specification has been objected to because the amino acid sequences in Figures 8A and 8B are not included in the Sequence Listing.

Included herewith is a substitute Sequence Listing that contains the amino acid sequences shown in Figures 8A and 8B. Also included herewith is an amendment to the specification wherein the Brief Description of the Drawings has been amended to include the new sequence identifiers. In view of the substitute Sequence Listing and the amendment to the specification, reconsideration and withdrawal of this objection is requested.

E. At paragraph 6d of the Office Action, the specification has been objected to because the trademark Titertek® is neither capitalized nor accompanied by generic terminology.

Included herewith is an amendment to the specification wherein the trademarked terms in paragraphs [194] and [196] have been capitalized. The generic terminology "plate reader" is already present in the noted paragraphs. In view of the amendment to the specification, reconsideration and withdrawal of this objection is requested.

II. Claim Rejections Under 35 U.S.C. §112

A. At paragraph 8 of the Office Action, claims 59 and 60 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The Examiner states that the recitation of "improved antibody or epitope binding fragment thereof" is indefinite because the term "improved" is not defined by the claim.

Included herewith is an amendment to claims 59 and 60 wherein the antibodies encompassed within the scope of the claims have "increased binding affinity" for CD33 compared to a first antibody.

In view of the amendment to the claims, claims 59 and 60 are definite as written and Applicants respectfully request reconsideration and withdrawal of this rejection.

B. At paragraph 10 of the Office Action, claims 1-14, 17-32, and 59-62 are rejected under 35 U.S.C. §112, first paragraph, as being non-enabled.

Specifically, the Examiner states that while the claims are enabled for an antibody or antibody fragment that specifically binds to CD33, comprising the six CDRs of SEQ ID NOs: 1-6, or comprising the heavy and light chain variable domains of SEQ ID Nos: 7 & 9, and 8 & 10, respectively, they are not enabled for:

(i) an antibody or fragment that comprises at least one CDR selected from SEQ ID NOs:1-6,

(i) an antibody or fragment that comprises (a) all six CDRs, (b) the heavy chain variable region of SEQ ID NO: 7 or 9, or (c) the light chain variable region of SEQ ID NO:8 or 10, wherein the antibody or fragment does <u>not</u> bind CD33,

(iii) a heavy chain variable region having at least 90% to 95% sequence identity to SEQ ID NO: 7 or 9 or a light chain variable region having at least 90% or 95% sequence identity to SEQ ID NO:8 or 10, wherein the antibody or fragment does not bind CD33, or

(iv) an improved antibody comprising at least one mutation, deletion, insertion, or addition that binds CD33.

In part (i) of the rejection, with respect to antibody fragments comprising at least one CDR, included herewith is an amendment to claim 1 such that the antibodies encompassed within the scope of the claim include those antibodies and epitope-binding fragments that specifically bind CD33 and comprise a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises the three CDRs represented by SEQ ID NOs: 1-3. The skilled artisan would be readily enabled to practice the full scope of the invention as recited in amended claim 1.

In parts (ii) and (iii) of the rejection, the Examiner states that the specification does not provide support for antibodies and homologues that "do not bind CD33." Included herewith is an amendment to claim 2 such that each of the pending claims now recite antibodies that bind CD33. The skilled artisan would be readily enabled to practice the full scope of the invention as recited in amended claim 2.

As to part (iv) of the rejection, the Examiner states improved antibodies comprising at least one mutation, deletion, insertion, or addition, and that binds CD33, are not supported by the specification.

Applicants note that the specification exemplifies an isolated antibody that binds to CD33. The isolated antibody was sequenced and humanized, and was determined to have heavy chain variable region sequences which are set forth in SEQ ID NOs: 7 (murine) and 9 (humanized), and light chain variable region sequences which are set forth in SEQ ID NOs: 8 (murine) and 10 (humanized). The specification also exemplifies functional equivalents of these antibodies (such as homologues, and mutants with deletions and insertions) produced through changes within the variable and/or constant region sequences that flank a particular set of CDRs (paragraph 91) or in the CDRs themselves (paragraph 97). The sequences of the CDRs are set

forth in SEQ ID NOs:1-6 and are encompassed within the heavy chain and the light chain variable region sequences set forth above. The specification teaches that procedures for making antibody homologues and mutants is routine in the art, and provides an assay for determining binding activity of the antibody to the CD33.

Applicants respectfully traverse the Examiner's position regarding the enablement of the functional equivalents encompassed within the scope of the claims. In particular, the skilled artisan would understand that changes to the heavy and light chain variable regions of the antibodies of the present invention could be made without changing the specificity of the antibodies. Therefore, the functional equivalents of the present application are fully enabled.

In particular, the claims recite homologues having homology to only the variable regions of the heavy and light chains, thus the genus of homologs recited in the claims is limited to a small, well-defined genus. Indeed, the claims only encompass homologues of four specific sequences - SEQ ID NOs:7-10.

In addition, Figures 16A and B of the application provide specific examples of humanized sequence homologs of the variable region sequences of the light chain (e.g., SEQ ID NO: 9) and of the heavy chain (e.g., SEQ ID NO: 10). Additionally, the results of the competitive binding studies between the murine and humanized My9-6 antibodies shown in Figure 18 demonstrate that humanized My9-6 antibodies can compete equally well for CD33 binding as murine My9-6 antibody.

Furthermore, paragraph [97] of the specification includes citations to a number of publications that teach how amino acid changes at various positions of the CDR regions of the antibody sequence can be made.

Finally, Applicants note that Examples 2 and 3 of the specification provide a detailed explanation of how the specific amino acids that were used to replace the murine My9-6 antibody variable region surface residues were chosen, as well as a detailed explanation of the methods use to construct, test, and use the homologs.

Accordingly, in view of the small, well-defined genus of sequences that are encompassed within the scope of the claims, the detailed description of the means by which the homologues and mutants can be made, the disclosed assay for testing the binding activity of the homologues and mutants, and the extensive knowledge in the art, the skilled artisan would be readily enabled to practice the full scope of the invention recited in the claims.

In view of the comments above and the amendments to the claims, each of claims 1-14, 17-32, and 59-62 is fully enabled, and Applicants respectfully request reconsideration and withdrawal of this rejection.

III. Claim Rejections Under 35 U.S.C. §102

A. At paragraph 12 of the Office Action, claims 1-8 and 15 are rejected under 35 U.S.C. §102(b) as being anticipated by Weitzhandler et al. (1994).

The Examiner states that Weitzhandler teaches a murine monoclonal antibody My9-6 that is identical to the murine monoclonal antibody comprising the heavy and light chain variable regions of SEQ ID NOs: 7 and 8, respectively, recited in the claims, and that the antibody is inclusive of the CDRs of SEQ ID NOs: 1-6. The Examiner reasons that because Weitzhandler teaches the claimed antibody, it necessarily comprises the heavy and light chain variable region of SEQ ID NOs: 7 and 8, and binds CD33.

Applicants respectfully traverse the instant rejection for the following reasons.

Weitzhandler teaches a murine monoclonal antibody, termed My9-6, that is derived from ascites fluid (see Abstract). Weitzhandler also teaches that the antibody was obtained from ImmunoGen Inc., the assignee of the instant application (third paragraph, col. 2., page 1670). Weitzhandler does not, however, provide any information regarding the identity of the antigen to which the My9-6 antibody binds. While reference to CD33 is made in the publication (second paragraph of the Introduction), this discussion is only background discussion regarding the glycosylation of the antibody. Weitzhandler does not provide, either explicitly or implicitly, the identity of the specific antigen bound by the My9-6 antibody.

As a result, Weitzhandler is not sufficiently enabling to serve as prior art against the claims. In order for a cited document to be anticipatory under §102, it must be sufficiently enabled. Specifically, MPEP § 2121.01 provides:

> The disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation. citing *Elan Pharm., Inc. v. Mayo Found. For Med. Educ. & Research*, 346 F.3d 1051, 1054 (Fed. Cir. 2003)...A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention. citing *In re Donohue*, 766 F.2d 531 (Fed. Cir. 1985).

emphasis added.

As Weitzhandler merely describes the glycosylation of a random antibody termed "My9-6", Weitzhandler does not contain a sufficiently enabling disclosure of the murine My9-6 antibody of the present application. Specifically, Weitzhandler does not characterize the antibody nor disclose any binding activity. Indeed, Weitzhandler is completely devoid of any disclosure that would enable a skilled artisan to use the publication's description of the antibody to make the claimed invention without undue experimentation.

Moreover, as indicated at paragraph 245 of the pending application, the My9-6 antibody of the present invention was not deposited in the ATCC until November 7, 2002. Therefore, the antibody itself was not publicly available as of the 1994 publication date of Weitzhandler.

Accordingly, Weitzhandler does not anticipate the claimed invention and Applicants respectfully request reconsideration and withdrawal of this rejection.

B. At paragraph 13 of the Office Action, claims 1-8, 15 and 17-28 are rejected under 35 U.S.C. §102(b) as being anticipated by R&D Focus Drug News (November 12, 2001).

The Examiner states that R&D Focus Drug News teaches the anti-CD33 murine monoclonal antibody My9-6 linked to the maytansinoid drug DM1. The Examiner further states that the My9-6 antibody disclosed in R&D Focus Drug News is identical to the claimed murine

monoclonal My9-6 antibody comprising the heavy and light chain variable regions of SEQ ID NOs: 7 and 8, respectively, and is inclusive of the CDRs of SEQ ID NOs: 1-6. Furthermore, the Examiner states that because R&D Focus Drug News discloses that the My9-6-DM1 immunoconjugate eliminated human tumor xenografts in mice, a skilled artisan would recognize that the administered immunoconjugate was necessarily present in the composition or the pharmaceutical composition comprising a pharmaceutically acceptable agent.

Applicants respectfully traverse the instant rejection for the following reasons.

Applicants note that R&D Focus Drug News has a publication date of November 12, 2001, which is less then one year before the November 7, 2002 filing date of the priority application (U.S. provisional application number 60/424,332) which fully supports the pending claims. Therefore, R&D Focus Drug News may not serve as legally-effective prior art under §102(b) against the claims of the present invention.

Applicants also enclose herewith a Declaration Under 37 C.F.R. §1.132 by the inventors, stating that the disclosure of R&D Focus Drug News regarding the My9-6 antibody is the work of the inventors, and therefore not the work of "another" as required under §102(a).

In view of these comments and the Declaration, Applicants respectfully request reconsideration and withdrawal of this rejection.

C. At paragraph 14 of the Office Action, claims 1-8, 15, and 17-29 are rejected under 35 U.S.C. §102(b) as being anticipated by CML NewsBytes (October 24, 2001).

The Examiner's basis for the rejection is substantially similar to his rejection based on R&D Focus Drug News.

Applicants respectfully traverse the instant rejection for the following reasons.

CML NewsBytes merely provides the name of a drug. It is does not indicate whether the named drug comprises an antibody, nor does it provide any information regarding the identity of the antigen to which the drug binds.

As a result, CML NewsBytes is not sufficiently enabling to serve as prior art against the claims. In order for a cited document to be anticipatory under §102, it must be sufficiently enabled. Specifically, MPEP § 2121.01 provides:

> The disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation. citing *Elan Pharm., Inc. v. Mayo Found. For Med. Educ. & Research*, 346 F.3d 1051, 1054 (Fed. Cir. 2003)...A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention. citing *In re Donohue*, 766 F.2d 531 (Fed. Cir. 1985).

emphasis added.

As CML NewsBytes merely mentions a drug termed "My9-6-DM1", CML NewsBytes does not contain a sufficiently enabling disclosure of the murine My9-6 antibody of the present application. Specifically, CML NewsBytes does not characterize the antibody nor disclose any binding activity. Indeed, CML NewsBytes is completely devoid of any disclosure that would enable a skilled artisan to use the publication's description of the drug to make the claimed invention without undue experimentation.

Moreover, as indicated at paragraph 245 of the pending application, the My9-6 antibody of the present invention was not deposited in the ATCC until November 7, 2002. Therefore, the antibody itself was not publicly available as of the 2001 publication date of CML NewsBytes.

Accordingly, CML NewsBytes does not anticipate the claimed invention and Applicants respectfully request reconsideration and withdrawal of this rejection.

D. At paragraph 15 of the Office Action, claims 1-8, 15 and 17-29 are rejected under 35 U.S.C. §102(a) as being anticipated by Lutz et al. (Proceedings of the American Association for Cancer Research Annual Meeting, Vol. 43, p. 912, March 2002) or by Goldmacher et al. (Proceedings of the American Association for Cancer Research Annual Meeting, Vol. 43, p. 254, March 2002).

The Examiner's basis for the rejection is substantially similar to his rejection based on R&D Focus Drug News.

Applicants enclose herewith two Declarations Under 37 C.F.R. §1.132 by the inventors, one with regard to each of the Abstracts, stating that the disclosures in the Abstracts regarding the My9-6 antibody is the work of the inventors, and therefore not the work of "another" as required under §102(a). Therefore, neither of the Abstracts may serve as legally-effective prior art under §102(a) against the claims of the present invention.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

IV. Claim Rejections Under 35 U.S.C. §103

At paragraph 17 of the Office Action, claims 17-32 are rejected under 35 U.S.C. §103(a) as being unpatentable over Goldenberg et al. (U.S. Patent No. 6,759,045) in view of R&D Focus Drug News.

The Examiner states that Goldenberg teaches (1) anti-CD33 antibodies and immunoconjugates thereof for the treatment of leukemia where the immunoconjugates comprise a drug or is labeled with a fluorescent or chromogenic agent, and (2) pharmaceutical compositions comprising the anti-CD33 antibodies or immunoconjugates thereof and a pharmaceutically acceptable carrier. The Examiner admits that Goldenberg does not teach the presently claimed antibody or conjugates thereof.

The Examiner goes on to state that R&D Focus Drug News teaches the anti-CD33 My9-6 antibodies as recited in the pending claims.

The Examiner concludes that a skilled artisan would have been motivated and would have had a reasonable expectation of success to combine the anti-CD33 My9-6 antibody taught by R&D Focus Drug News with various chemotherapeutic drugs of Goldenberg to produce pharmaceutical compositions comprising the My9-6 antibody or conjugates thereof and a pharmaceutically acceptable carrier for treatment of leukemia.

As set forth above, the disclosure of R&D Focus Drug News regarding the My9-6 antibody is the work of the present inventors. Accordingly, R&D Focus Drug News may not serve as legally-effective prior art against the claims of the present application.

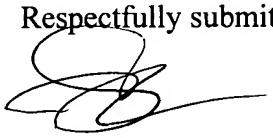
As Goldenberg alone does not teach each and every element of the rejected claims, the Examiner has not established a *prima facie* showing of obviousness. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

V. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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